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April 9, 2007

BY E-FILING

The Honorable Joseph J. Farnan, Jr.
United States District Court
844 King Street
Wilmington, DE 19801

Re: *The Procter & Gamble Co. v. Teva Pharmaceuticals USA, Inc.*,
C.A. No. 04-940-JJF

Dear Judge Farnan:

We represent defendant Teva Pharmaceuticals USA, Inc., in the above-captioned case, which was tried before your Honor in November 2006. A principal issue in the case is whether a particular chemical compound, risedronate, also referred to as “3-pyr EHDP,” would have been obvious in view of a disclosure of a closely related compound, “2-pyr EHDP.” Since briefing in this case was completed, the Federal Circuit decided *Pfizer, Inc. v. Apotex, Inc.*, 2007 U.S. App. LEXIS 6623 (March 22, 2007) (copy attached), which likewise involved the issue whether a particular pharmaceutical compound would have been obvious. The court’s treatment of obviousness in that case is instructive with respect to the issues here.

In *Pfizer*, the issue was whether the compound amlodipine benzene sulphonate (or amlodipine “besylate”), which is the active ingredient in the drug Norvasc, would have been obvious. Amlodipine besylate is a salt, which means that it is made by reacting amlodipine, a base, with benzene sulphonic acid, just as sodium chloride (table salt) can be made by reacting sodium hydroxide, a base, with hydrochloric acid. Amlodipine was an old compound, and the prior art disclosed both that compound and certain of its salts. No prior art reference, however, disclosed the besylate salt, although the prior art did disclose besylate as one of more than 50 anions that could in general be used to make pharmaceutically acceptable salts.

In reversing the district court’s holding that the compound would not have been obvious, the Federal Circuit first addressed the burdens of proof. The court held that although the party challenging the patent bears the burden of proving the “factual elements” of invalidity, “once a challenger has presented a prima facie case of invalidity, the patentee has the burden of going forward with rebuttal evidence.” 2007 U.S. App. LEXIS 6623 at *24. This statement confirms the correctness of Teva USA’s allocation of the burdens of proof in this case. (See Teva USA’s Post-Trial Reply Brief, D.I. 103, at 2-4.)

Of particular relevance, however, is the Federal Circuit’s discussion of “reasonable probability” or “reasonable expectation” of success, which is the standard for measuring prima

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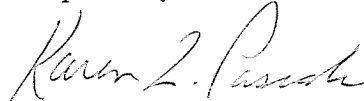
facie obviousness. The district court had found that "it was generally unpredictable as to whether a particular salt would form and what its exact properties would be." The Federal Circuit accepted the finding, but nevertheless held that this unpredictability does not negate reasonable probability of success:

The problem with the district court's ultimate conclusion of non-obviousness based on that factual finding, however, is that case law is clear that obviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success. . . . Indeed, a rule of law equating unpredictability to patentability, applied in this case, would mean that any new salt . . . would be separately patentable, simply because the formation and properties of each salt must be verified through testing. This cannot be the proper standard. . . .

Id. at *25.

P&G's argument that risedronate is not prima facie obvious in view of 2-pyr EHDP rests primarily on its assertion that the art was not "predictable," and that a person skilled in the art would not have known in advance that risedronate would be highly active to inhibit bone resorption. In essence, P&G makes the same argument the Federal Circuit rejected in *Pfizer*: unpredictability equates to patentability, and that in view of the alleged unpredictability of bisphosphonates, each is separately patentable because the properties of each must be verified by testing. P&G, however, does not dispute that the molecular structure of risedronate is almost identical to that of 2-pyr EHDP, which exhibited excellent activity and a very favorable therapeutic ratio. Nor does it dispute that with respect to bisphosphonates, the prior art taught that (1) they are active as a class, (2) those that include a hydroxy function in the molecular "head" (such as risedronate) tend to be more active than those that do not, and (3) including a nitrogen atom in the "tail" of the molecule (as is found in risedronate) generally improves activity. Thus, even if the properties of individual bisphosphonates could not be precisely predicted and the level of activity of risedronate could not be verified without testing, a person skilled in the art still would have had a reasonable expectation that risedronate would exhibit the desired activity. That reasonable expectation is all that is required to establish risedronate's prima facie obviousness.

Respectfully submitted,



Karen L. Pascale (No. 2903)

Enclosure

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